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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,726	11/28/2000	Gyula Hadlaczky	24601-402E	7776

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EXAMINER

HELMER, GEORGIA L

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 01/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,726

Applicant(s)

HADLACZKY ET AL.

Examiner

Georgia L. Helmer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 50-52,58-61,65-67 and 72 is/are pending in the application.
- 4a) Of the above claim(s) 58-61,65-67 and 72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 50-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election, Paper No. 15, filed 3 October 2002. Applicant elects Group IV claims 50-52 as drawn to plant protoplasts and SATACs, with traverse. Claims 50-52, 58-61, 65-67, and 72 are pending. Claims 1-49, 53, 54, 62-64, 68-71, and 73, drawn to a nonelected inventions, are cancelled. Claims 50-52 are examined in this Office Action.

Applicant traverses, stating primarily that Group IV, VI, and VIII are related as genus/species. Applicant's traversal has been considered and is unpersuasive because protoplasts and cells are not related as genus/species. They are distinct, physically, biochemically, and structurally, and a protoplast is not a plant cell. Applicant even points out that a plant cell has a cell wall, which a protoplast does not. For the reasons stated in the restriction requirement and because it would be an undue burden, the claims are properly restricted. Furthermore, the sequences of Group II are also properly restricted, since they differ structurally and would each require a separate search, regardless of whether they encode a protein.

This restriction is made Final.

Information Disclosure Statement

2. Initialed and dated copies of Applicant's IDS forms 1449, Paper No. 7 (5/16/01), 8 (8/27/01), 9 (9/10/01), 10 (12/4/01), 12 (4/9/02), 13 (6/6/02), 14 (9/4/02), and 16 (10/10/02) are attached to the instant Office action.

Claim Rejections - 35 USC § 112-second

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 50, "the protoplast cell" lacks antecedent basis.

Claim 50 is also an incomplete method step, because essential steps are not recited in the method.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112.1 Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 50-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 50-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for any SATAC (satellite artificial chromosome) in any plant protoplast or any transgenic plant.

The nature of the invention: Applicant's invention relates to methods for preparing protoplasts containing artificial chromosomes, and growing the protoplast to produce a transgenic plant.

Applicant discloses an animal SATAC. Applicant's claims are drawn to any SATAC. Mammals, and animals, are not representative of plants in terms of chromosomes and chromatin structure. In animals and in yeast, satellite DNA is AT-rich, whereas plant satellite DNA tends to be GC-rich (Ferl, R et al in Buchanin, et al. Biochemistry & Molecular Biology of Plants (2000) American Society of Plant Physiologists, Rockville Md 20855, page 324.) GC-rich DNA differs in physical properties from AT-rich DNA; GC rich DNA is more compact and dense, reflecting its more highly hydrogen-bonded structure (Lehninger, A. Biochemistry. 2nd edition, 1976, Worth Publishers, New York. p 864). It is unclear how compact, densely H-bonded DNA affects SATAC activity and function. Furthermore, telomeres, origin of DNA replication and a centromere are required for function of a SATAC (Willard, HF,

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Science, 290, pps 1308-9, 2000). It is unclear what telomeres, origin of DNA replication and centromere are necessary for other than animal SATACs, whether additional components are required, or how to isolate or construct functional SATAC in all cells, or non-mammalian cells. Plant centromeres have yet to be physically constructed or isolated. However, plant centromeres of Arabidopsis have been defined by genetic and sequence analysis (Copenhaver, et al, Science, 286, December, 1999, pages 2468-2474). Centromeres of artificial chromosomes show some species-specific behavior in animal systems (Willard, HF, Science, 290, pps 1308-9, 2000; Shen, et al, Current Biology 10, 31-34, 2000; Telenius, et al, Chromosome Research 7, pages 3-7, 1999; Ferl, R et al in Buchanan, et al. Biochemistry & Molecular Biology of Plants (2000) American Society of Plant Physiologists, Rockville Md 20855, page 324,5).

It is unpredictable that plants, from a totally different Kingdom than animals, would have centromeres which are structurally and biochemically the same as those of animals. Neither the Applicant, nor the prior art, teach how to isolate or make plant centromeres, nor how to make a SATAC having a plant centromere. Rather it is predictable that plant centromeres would differ from animal centromeres, since animal centromeres differ among themselves and show species-specific behavior. Patterns of heterochromatin differ between animal and plants, with animals showing heterochromatization in telomeres, centromeric, and pericentrometic regions. In plants, however, heterochromatin is located at the nucleolar organizer, and at the chromosome knobs. See Avramova, Plant Physiology, 2002, vol 129, pages 40-49. Plant

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heterochromatin differs from animal heterochromatin in the absence of proteins similar to known heterochromatin proteins, location of potentially active genes in the knob structures and in the pericentromeric regions of plant genome, and different chromosomal environments for collinear genes in related species (Avramova, op cit, p 41). In fact plants have a family of 20 methyltransferase enzymes unique to plants, putatively representing host factors necessary for proper function of plant systems and not required in other systems. Therefore, given that plant satellite DNA, plant centromeres and plant heterochromatin differ from their animal counterparts, it is unpredictable that a plant SATAC, consisting of those components, would function as desired in the claimed invention.

Re: expression of a gene product from a SATAC comprising heterologous DNA:

Simple heterologous expression constructs in animal host systems are clearly structurally different from heterologous expression constructs in other host systems, including plants. Required are different promoters, enhancers, codon optimization, termination regions, and other regulatory regions. One of skill in the art would expect a SATAC constructed for mammalian cells to differ from a SATAC functional in a non-mammalian cell. SATACs are much more complex, than just the mere heterologous expression system, and require manipulation of much larger size DNA. The transfer of large pieces of DNA between cells is a major problem in artificial chromosome technology (Brown, Trends in Biotech, 2000, vol 18, p 403; Perez, et al, Trends in Biotech, 2000, 18, 402-3; Willard, HF, Science, 290, 1308-9, 2000; Hadlaczky, Curr. Opin. Mol Ther, 2001, vol 3, pages 125-32, p 129).

Re: *The amount of Guidance given:* It is unclear what regions of Applicant's animal SATAC should be retained, and what regions should be modified, to obtain a SATAC that would be operable in a non-mammalian cell. The art of artificial chromosome technology is in its infancy (Willard, HF, Science, 290, pps 1308-9, 2000, final paragraph). Therefore, much greater guidance would be required. Applicant teaches an animal SATAC in a mammalian cell. Applicant does not address any of the issues set forth above. While one skilled in the art can readily make necessary changes to Applicant's mammalian SATAC to generate a non-mammalian SATAC, guidance is required as to what those changes are. To require one skilled in the art to randomly make changes to Applicant's animal SATAC, or to generate their own SATAC constructs without guidance as to how inoperable embodiments can be readily eliminated other than by trial and error, is an invitation to experiment, requiring excessive and undue experimentation. Accordingly Applicant has not enabled a SATAC generated from any source, much less as commensurate in scope with the claims.

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Applicant discloses human, mouse, and hamster cells. The claims are drawn to a method of producing any plant protoplast and growing it into a transgenic plant. While mammalian and nonmammalian cells have been extensively used to express heterologous constructs, the constructs must be recognized by the cell machinery. Otherwise, the construct would be degraded or removed from the cell. No construct to date is universally recognized in all cells. One skilled in the art would expect that a SATAC construct for a mammalian cell would also differ from a SATAC construct for a plant protoplast.

Applicant does not disclose that the SATAC of the instant application is universally adapted to be operable in all cell types. Applicant has only shown that Applicant's SATAC is operable in a mammalian cell. It is unpredictable that Applicant's SATAC would be operable in all cell types. Accordingly, Applicant has only enables Applicant's SATAC for a mammalian cell. Thus Applicant is not enabled for using any SATAC in any plant protoplast, or any transgenic plant

Remarks

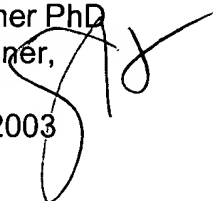
6. No claim is allowed.
7. The claims are free of the prior art.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

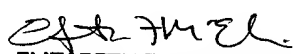
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia Helmer PhD
Patent Examiner,
Art Unit 1638
January 10, 2003




ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800